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## EFFECT OF HISTAMINE ON FREE FATTY ACIDS IN RUMINANTS<sup>1</sup>

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In a previous work (Neumark, 1967) it was shown that under certain conditions histamine, introduced *per os* in rams, affected the appetite strongly. Later, Neumark and Tadmor (1968) demonstrated that the site of absorption of histamine in ruminants was the omasum. This paper deals with the effect of omasal or intravenous infusions of histamine on the level of plasma free fatty acids (FFA) in ruminants, and the effect of the increased level of FFA on the milk fat percentage in cows.

### *Experiment with a steer*

The 20-month-old castrated steer « Aluf » was fitted with an omasal fistula according to the method of Tadmor and Neumark (1972). The fistula was established 10 months prior to the experiments described below. In all experiments 500 ml distilled water containing 1.5 g histamine-2HCl and 16 ml formic acid were infused into the omasum by means of a cannula inserted into the omasum. For determination of FFA, blood was withdrawn from the jugular vein into evacuated glass tubes, containing sodium fluoride or heparin as anticoagulants. After

collection of the blood, the tubes were immediately ice-cooled and centrifuged after 2-3 h. The plasma was kept at  $-20^{\circ}\text{C}$  until further assay of FFA. In all experiments blood was collected immediately before the histamine infusions, the concentrations of FFA were determined and a relative value of 100% was assigned to them. Concentrations of FFA of blood samples, taken after histamine infusions, were compared with those of samples taken before infusions, and calculated as percentage of the latter. Sham infusions were carried out to investigate the effect of the infusion *per se* on the FFA levels. No effect of sham infusion on the level of FFA was found.

The fatty acids were assayed by extracting 1.5 ml plasma according to the method of Muto and Gibson (1970) and isolated by thin-layer chromatography according to Storry and Tuckley (1967). The silica gel strips containing the FFA were scraped from the glass plates, the fatty acids methylated by diazomethane and quantitatively assayed by gas liquid chromatography.

### *Experiment with lactating cows*

Four Israeli-Holstein cows were divided into two groups. Two cows, N<sup>o</sup> 1 and 2, were infused *intra venam jugularis* five times

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with 5 ml of Ringer solution, containing 5 mg histamine-2HCl. Infusions were carried out during 1.5 hours between the morning and noon milkings, at intervals of about 20 min. The two other cows, N° 3 and 4, served as control. Blood was withdrawn simultaneously from the jugular (*v. jug.*) and subcutaneous abdominal (*v. abd.*) veins of all four cows; the first time before the start of the infusions and the second time 20 min. after the fifth infusion of histamine in treated cows. Representative samples of the morning and noon milkings of each cow were taken and their fat percentage determined by the « Gerber method ».

Plasma glucose was determined by the glucose oxydase-peroxidase method (Sigma, St Louis, Mo., USA) and plasma FFA by a method described in the first part of this paper.

## Results and Discussion

### Steer

After infusion of histamine and formic acid FFA concentrations increased (table 1), regardless of the pre-infusion concentration of FFA. The first samples in Experiments 1 and 2 were collected at a relatively short time after infusion evincing the fast absorption of the histamine solution from the omasum. The lasting effect of histamine, demonstrated by the continuously high level of FFA — even more than 4 hours after infusion (second collection of Exp. 3 and 4, table 1), — indicates the strong effect of histamine on the concentration of FFA and a relatively long-lasting flow of small amounts of the infused histamine from the omasum into the blood stream. The assumption that the relatively large dose of infused histamine

Table 1. — Plasma free fatty acids (FFA) concentrations<sup>1</sup> after infusion of histamine and formic acid<sup>2</sup> into the omasum of steer « Aluf »

Experiment N°	Time after histamine infusion (min.)	Plasma FFA concentration (%)
1	13	158.9
2	14	125.3
2	118	158.6
3	80	178.6
3	260	116.7
4	88	172.6
4	260	136.4

<sup>1</sup> Values calculated as percentage of pre-infusion concentrations of plasma FFA (100%).

<sup>2</sup> 500 ml distilled water containing 1.5 g histamine-2HCl and 16 ml formic acid.

Mean plasma FFA concentration  $\pm$  SE before infusion: 3496.3  $\pm$  854 mcg/100 ml plasma.

Table 2. — Concentrations of plasma glucose, FFA and milk fat of lactating cows before and after intravenous infusions\* of histamine-2HCl

Cow N°	Treatment	Glucose (mg/100 ml)	FFA (mg/100 ml)		Milk fat (%)
			<i>v. jug.</i>	<i>v. abd.</i>	
1	Before histamine infusion	53	2.22	2.30	2.1 <sup>m</sup>
	After histamine infusion	97	3.11	2.84	2.3 <sup>n</sup>
2	Before histamine infusion	34	2.43	4.68	2.1 <sup>m</sup>
	After histamine infusion	88	2.58	2.52	3.3 <sup>n</sup>
3	Control	48	2.65	3.52	2.8 <sup>m</sup>
		50	2.29	2.92	3.2 <sup>n</sup>
4	Control	47	2.24	2.77	2.9 <sup>m</sup>
		48	2.37	2.45	2.6 <sup>n</sup>

\* Five infusions of 5 ml of Ringer solution, containing 5 mg histamine-2HCl, given at intervals of 20 min.

<sup>m</sup> Fat percentage of morning milk (before experiment).

<sup>n</sup> Fat percentage of noon milk (after experiment).

is released from the omasum in only small amounts but for a long period is supported by the findings of the following experiments with lactating cows, which reacted strongly but for only a short time to small single doses of a few mg of histamine, infused into the vena jugularis.

#### Cows

The strong reaction to histamine infusions is indicated by the sharp rise of the level of plasma glucose in cows no. 2 (table 2). An increase of plasma FFA levels was to be expected according to the results with the steer. Infusion of histamine in cow 1 increased plasma FFA levels markedly in samples taken from the *v. jug.* as well as from the *v. abd.*, whereas the plasma FFA

levels of the control cows remained almost unchanged. Changes in milk fat percentage of cow 1 and the control cows, 3 and 4, were only slight.

In contrast, in cow 2 the plasma FFA level after histamine infusions dropped sharply in the sample from the *v. abd.* but remained virtually unchanged in that from the *v. jug.* The percentage of milk fat of this cow increased markedly after histamine infusions and it appears that the increased milk fat percentage (about 50%) may be connected with net uptake of FFA by the udder, thereby preventing an increase of plasma FFA concentrations following the histamine infusions. The failure to utilize increased FFA concentrations for milk fat synthesis, as found in cow 1, demands further investigation.

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